AMENDED CLAIM SET:

1. (currently amended) A method of preparing the chiral (±) isomers of indole-2,3-dione-3-oxime compounds ~~derivatives~~, which method comprises the sequential steps of:

(i) reacting an 8-amino-1,2,3,4-tetrahydro-isoquinoline with chloral hydrate and hydroxylamine hydrochloride to give an *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide;

(ii) adding sulphuric acid to the *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide obtained in step (i) to provide a 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline; and

(iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline obtained in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone to obtain the desired chiral end product, i.e. enantiopure (R)- or (S)-2-[2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid.

2. (currently amended) The method of claim 1, which method further comprises the step of

(a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc-hydroxylamine to give enantiopure (*S*) or (*R*) α-*N,N*-diBoc-aminoxy-γ-butyrolactone;

followed by ~~steps (i) to (iii) of claim 1~~ the sequential steps of:

(i) reacting an 8-amino-1,2,3,4-tetrahydro-isoquinoline with chloral hydrate and hydroxylamine hydrochloride to give an *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide;

(ii) adding sulphuric acid to the *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide obtained in step (i) to provide a 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline; and

(iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline obtained in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone to obtain

the desired chiral end product, i.e. enantiopure (R)- or (S)-2-[2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid.

3. (currently amended) The method of claim 1, which method further comprises the step of

(b) subjecting *N,N*-diBoc-*O*-benzylhydroxylamine to hydrogenation to give *N,N*-diBoc-hydroxylamine;

followed by step (a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc-hydroxylamine to give enantiopure (*S*) or (*R*) α-*N,N*-diBoc-aminoxy-γ-butyrolactone; and

followed by ~~steps (i) to (iii) of claim 1~~ the sequential steps of:

(i) reacting an 8-amino-1,2,3,4-tetrahydro-isoquinoline with chloral hydrate and hydroxylamine hydrochloride to give an *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide;

(ii) adding sulphuric acid to the *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide obtained in step (i) to provide a 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline; and

(iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline obtained in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone to obtain the desired chiral end product, i.e. enantiopure (R)- or (S)-2-[2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid.

4. (currently amended) The method of claim 1, which method further comprises the step of

(c) converting *O*-benzylhydroxylamine into *N,N*-diBoc-*O*-benzylhydroxylamine using Boc_2O;

followed by step (b) subjecting *N,N*-diBoc-*O*-benzylhydroxylamine to hydrogenation to give *N,N*-diBoc-hydroxylamine;

followed by step (a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc-hydroxylamine to give enantiopure (*S*) or (*R*) α-*N,N*-diBoc-aminoxy-γ-butyrolactone; and

followed by ~~steps (i) to (iii) of claim 1~~ the sequential steps of:

(i) reacting an 8-amino-1,2,3,4-tetrahydro-isoquinoline with chloral hydrate and hydroxylamine hydrochloride to give an *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide;

(ii) adding sulphuric acid to the *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide obtained in step (i) to provide a 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline; and

(iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline obtained in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone to obtain the desired chiral end product, i.e. enantiopure (R)- or (S)-2-[2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid.

5. (currently amended) The method of claim 1, which method further comprises the step of

(d) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with tosyl chloride to give enantiopure (*S*) or (*R*) α-tosyloxy-γ-butyrolactone;

followed by step (c) converting *O*-benzylhydroxylamine into *N,N*-diBoc-*O*-benzylhydroxylamine using Boc_2O;

followed by step (b) subjecting *N,N*-diBoc-*O*-benzylhydroxylamine to hydrogenation to give *N,N*-diBoc- hydroxylamine;

followed by step (a) reacting enantiopure (*S*) or (*R*) α-hydroxy-γ-butyrolactone with *N,N*-diBoc followed by ~~steps (i) to (iii) of claim 1~~ the sequential steps of:

(i) reacting an 8-amino-1,2,3,4-tetrahydro-isoquinoline with chloral hydrate and hydroxylamine hydrochloride to give an *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide;

(ii) adding sulphuric acid to the *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide obtained in step (i) to provide a 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline; and

(iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline obtained

in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone to obtain the desired chiral end product, i.e. enantiopure (R)- or (S)-2-[2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid.

6. (cancelled).

7. – 11. (cancelled).

12. (cancelled).

13. (new) A method of preparing a chiral (±) isomer of an indole-2,3-dione-3-oxime compound, which method comprises the sequential steps of:

(i) reacting 4-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-5-yl)-*N,N*-dimethyl-benzenesulfonamide and hydroxylamine hydrochloride to give *N*-[5-(4-dimethylsulfamoyl-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-yl]-2-hydroxyimino-acetamide;

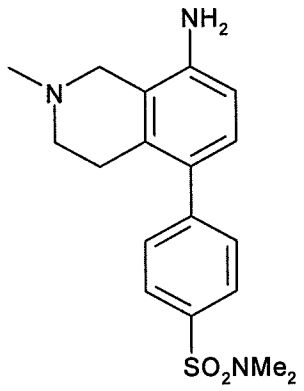
(ii) adding sulphuric acid to the *N*-[5-(4-dimethylsulfamoyl-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-yl]-2-hydroxyimino-acetamide obtained in step (i) to provide *N,N*-dimethyl-4-(8-methyl-2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinolin-5-yl)-benzenesulfonamide; and

(iii) reacting the *N,N*-dimethyl-4-(8-methyl-2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinolin-5-yl)-benzenesulfonamide obtained in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone to obtain the desired chiral end product, i.e. enantiopure (R)- or (S)-2-[5-(4-dimethylsulfamoyl-phenyl)-8-methyl-2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid,

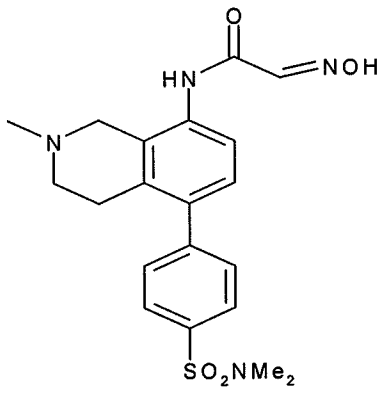
followed by recovery of the desired end product.

14. (new) A method of preparing the chiral (±) isomers of indole-2,3-dione-3-oxime compounds in accordance with claim 1, which method comprises the sequential steps of:

(i) reacting an 8-amino-1,2,3,4-tetrahydro-isoquinoline of the formula

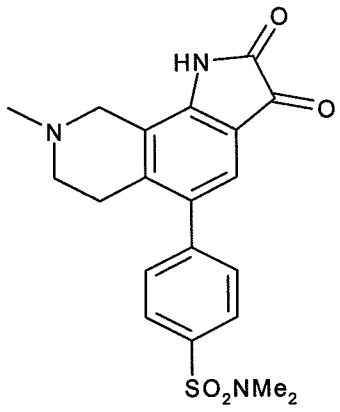


with chloral hydrate and hydroxylamine hydrochloride to give an *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide of the formula



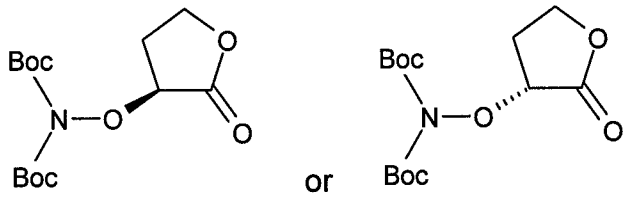
;

(ii) adding sulphuric acid to the *N*-(1,2,3,4-tetrahydro-isoquinolin-8-yl)-2-hydroxyimino-acetamide obtained in step (i) to provide a 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline of the formula

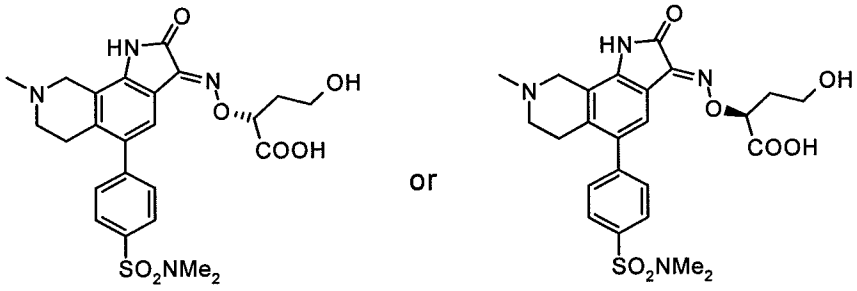


; and

(iii) reacting the 2,3-dioxo-2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2-h]isoquinoline obtained in step (ii) with chiral (enantiopure (*R*) or (*S*)) α-*N,N*-diBoc-aminoxy-γ-butyrolactone of the formula



to obtain the desired chiral enantiopure (R)- or (S)-2-[2-oxo-1,2,6,7,8,9-hexahydro-pyrrolo[3,2-h]isoquinolin-3-ylideneaminooxy]-4-hydroxy-butyric acid of the formula (IVA) or (IVB)



(IVA) **(IVB)**